CLAIMS

We claim:

1. An isolated T2R variant-specific nucleic acid molecule comprising at least about 10 contiguous nucleotides, spanning at least one SNP identified as new in Figure 1.

2. An array, comprising two or more nucleic acid molecules of claim 1.

3. The array of claim 2, comprising at least one nucleic acid molecule comprising at least about 10 contiguous nucleotides from T2R1, T2R3, T2R4, T2R5, T2R7, T2R8, T2R9, T2R10, T2R13, T2R14, T2R16, T2R38, T2R39, T2R40, T2R41, T2R43, T2R44, T2R45, T2R46, T2R47, T2R48, T2R49, T2R50, and T2R60, and spanning at least one SNP identified as new in Figure 1.

4. The array of claim 2, comprising at least one oligonucleotide from each T2R haplotype/allele listed in Table 7.

5. The array of any one of claims 2-4, which array is a microarray.

6. A collection of two of more isolated T2R variant-specific nucleic acid molecule, each comprising at least about 10 contiguous nucleotides spanning at least one T2R SNP position listed in Table 7.

7. The collection of claim 6, comprising at least one isolated T2R variant-specific nucleic acid molecule from T2R1, T2R3, T2R4, T2R5, T2R7, T2R8, T2R9, T2R10, T2R13, T2R14, T2R16, T2R38, T2R39, T2R40, T2R41, T2R43, T2R44, T2R46, T2R47, T2R48, T2R49, T2R50, and T2R60.

8. The collection of claim 6, comprising at least one isolated T2R variant-specific nucleic acid molecule from every SNP listed in Table 7.

9. The collection of claim 6, comprising at least one isolated T2R variant-specific nucleic acid molecule from each of SEQ ID NO: 49, 55, 57, 59, 63, 65, 67, 69, 71, 75, 77, 79, 81, 83, 85, 89, 91, 93, 95, 99, 101, 103, 105, 107, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 135, 139, 141, 147, 149, 151, 155, 157, 161, 163, 169, 173, 175, 177, 179, 181, 183, 187, 189, 191, 197, 199, 201, 203, 205, 209, 211, 213, 217, 219, 225, 227, 229, 231, 233, 235, 237, 241, 243, 245, 247, 249, 251, 253, 257, 259, and 263.

10. The collection of claim 9, wherein the isolated T2R variant-specific nucleic acid molecules have a sequence as shown in SEQ ID NO: 49, 55, 57, 59, 63, 65, 67, 69, 71, 75, 77, 79, 81, 83, 85, 89, 91, 93, 95, 99, 101, 103, 105, 107, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 135, 139, 141, 147, 149, 151, 155, 157, 161, 163, 169, 173, 175, 177, 179, 181, 183, 187, 189, 191, 197, 199, 201, 203, 205, 209, 211, 213, 217, 219, 225, 227, 229, 231, 233, 235, 237, 241, 243, 245, 247, 249, 251, 253, 257, 259, or 263.

11. The collection of claim 6, wherein each nucleic acid molecule is stored in a separate container.

12. The collection of claim 11, wherein the separate containers are wells of a microtiter plate or equivalent thereof.

13 The collection of any one of claims 6-12, wherein the nucleic acid molecules of the collection are affixed to a solid surface in an array.

14. The collection of claim 13, wherein the array is a microarray.

15. The microarray collection of claim 14, which comprises nucleic acid molecules having the sequence as set for in SEQ ID NO: 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, and 263.

16. The collection of claim 6, wherein the isolated T2R variant-specific nucleic acid molecule comprise:

(a) SEQ ID NOs: 47, 49, and 51;

(b) SEQ ID NOs: 53 and 55;

(c) SEQ ID NOs: 57, 59, 61 , 63, 65, 67, 69, and 71;

(d) SEQ ID NOs: 73, 75, 77, 79, 81, 83, and 85;

(e) SEQ ID NOs: 87, 89, 91, 93, and 95;

(f) SEQ ID NOs: 97, 99, 101, 103, 105, and 107;

(g) SEQ ID NOs: 109, 111, 113, 115, 117, 119, 121, and 123;

(h) SEQ ID NOs: 125, 127, 129, and 131;

(i) SEQ ID NOs: 133 and 135;

(j) SEQ ID NOs: 137, 139, and 141;

(k) SEQ ID NOs: 143, 145, 147, 149, and 151;

(l) SEQ ID NOs: 153, 155, 157, 159, 161, 163, and 165;

(m) SEQ ID NOs: 167 and 169;

(n) SEQ ID NOs: 171, 173, 175, and 179;

(o) SEQ ID NOs: 181, 183, and 185;

(p) SEQ ID NOs: 187, 189, 191, 193, 195, 197, and 199;

(q) SEQ ID NOs: 201, 203, 205, 207, 209, and 211;

(r) SEQ ID NOs: 213, 215, 217, and 219;

(s) SEQ ID NOs: 221, 223, 225, 227, 229, 231, 233, 235, and 237;

(t) SEQ ID NOs: 239, 241, 243, 245, 247, 249 and 251;

(u) SEQ ID NOs: 253, 255, 257, and 259;

(v) SEQ ID NOs: 261 and 263; or

(w) a combination of two or more of (a) through (v).

PCT/US2004/019489

17. An isolated T2R polypeptide isoform fragment, encoded by the nucleic acid molecule of claim 1.

18. An isolated T2R isoform polypeptide fragment comprising an amino acid sequence comprising at least 10 contiguous amino acids of SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 50, 56, 58, 60, 64, 66, 68, 70, 72, 76, 78, 80, 82, 84, 86, 90, 92, 94, 96, 100, 102, 104, 106, 108, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 136, 140, 142, 148, 150, 152, 156, 158, 162, 164, 170, 174, 176, 178, 180, 182, 184, 188, 190, 192, 198, 200, 202, 204, 206, 210, 212, 214, 218, 220, 226, 228, 230, 232, 234, 236, 238, 242, 244, 246, 248, 250, 252, 254, 258, 260, or 264, which fragment includes at least one amino acid variation as set forth in Figure 1 or Table 7.

19. An isolated T2R polypeptide isoform comprising an amino acid sequence selected from SEQ ID NO: 50, 56, 58, 60, 64, 66, 68, 70, 72, 76, 78, 80, 82, 84, 86, 90, 92, 94, 96, 100, 102, 104, 106, 108, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 136, 140, 142, 148, 150, 152, 156, 158, 162, 164, 170, 174, 176, 178, 180, 182, 184, 188, 190, 192, 198, 200, 202, 204, 206, 210, 212, 214, 218, 220, 226, 228, 230, 232, 234, 236, 238, 242, 244, 246, 248, 250, 252, 254, 258, 260, or 264.

20. An isolated nucleic acid molecule, encoding the T2R polypeptide isoform of claim 19.

21. A vector comprising the isolated nucleic acid molecule of claim 20.

22. A host cell comprising the vector of claim 21.

23. An isolated nucleic acid molecule comprising a nucleotide sequence for a T2R allele, wherein the nucleotide sequence is selected from SEQ ID NO: 49, 55, 57, 59, 63, 65, 67, 69, 71, 75, 77, 79, 81, 83, 85, 89, 91, 93, 95, 99, 101, 103, 105, 107, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 135, 139, 141, 147, 149, 151, 155, 157, 161, 163, 169, 173, 175, 177, 179, 181, 183, 187, 189, 191, 197, 199, 201, 203, 205, 209, 211, 213, 217, 219, 225, 227, 229, 231, 233, 235, 237, 241, 243, 245, 247, 249, 251, 253, 257, 259, or 263.

24. A vector comprising the isolated nucleic acid molecule of claim 23.

25. A host cell comprising the vector of claim 24.

26. A method of screening compounds useful for modulating bitter taste, comprising:

contacting a test compound with a host cell or membrane thereof that expresses a T2R taste receptor isoform encoded by the isolated nucleic acid molecule of claim 20; and

detecting a change in the expression of the nucleotide sequence or a change in activity of the T2R taste receptor, or detecting binding of the compound to the T2R taste receptor or detecting a change in the electrical activity of the host cell or a change in intracellular or extracellular cAMP, cGMP, IP3, or Ca^{2+} of the host cell.

27. The method of claim 26, wherein the gene product of said nucleotide sequence is fused to a sequence that facilitates localization to the cell membrane, wherein that sequence is at least 20 consecutive N terminal amino acids of a rhodopsin protein.

28. The method of claim 26, wherein the cell is a eukaryotic cell.

29. The method of claim 28 wherein the eukaryotic cell is a HEK293 cell.

30. The method of claim 26 wherein a change in intracellular Ca^{2+} is detected by measuring a change in a calcium-sensitive dye dependent fluorescence in the cell.

31. The method of claim 26 wherein a change in intracellular Ca^{2+} is detected by measuring a change in Fura-2 fluorescence in the cell.

32. The method of claim 26, which is a high throughput method, comprising:

contacting in parallel a test compound with a collection of host cells or membranes thereof each of which expresses a different T2R taste receptor isoform encoded by an isolated nucleic acid molecule comprising a nucleotide sequence for a T2R allele, wherein the nucleotide sequence is selected from SEQ ID NO: 49, 55, 57, 59, 63, 65, 67, 69, 71, 75, 77, 79, 81, 83, 85, 89, 91, 93, 95, 99, 101, 103, 105, 107, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 135, 139, 141, 147, 149, 151, 155, 157, 161, 163, 169, 173, 175, 177, 179, 181, 183, 187, 189, 191, 197, 199, 201, 203, 205, 209, 211, 213, 217, 219, 225, 227, 229, 231, 233, 235, 237, 241, 243, 245, 247, 249, 251, 253, 257, 259, and 263; and

detecting a change in the expression of at least one of the nucleotide sequences or a change in activity of at least one of the T2R taste receptors, or detecting binding of the compound to at least one of the T2R taste receptors or detecting a change in the electrical activity of at least one of the host cells or a change in intracellular or extracellular cAMP, cGMP, IP3, or Ca^{2+} of at least one of the host cells.

33. The method of claim 23, wherein the collection of host cells or membranes thereof are in the form of an array.

34. An *in vivo* method of screening compounds useful for modulating bitter taste, comprising:

contacting a test compound to a T2R taste receptor isoform encoded by the isolated nucleic acid molecule of claim 2; and

detecting a change in the activity of the T2R taste receptor, or detecting binding of the compound to the T2R taste receptor.

35. The method of claim 34, which is a high throughput method, comprising:

contacting in parallel a test compound with a collection of different T2R taste receptor isoforms encoded by the isolated nucleic acid molecules; and

detecting a change in the activity of at least one of the T2R taste receptors, or detecting binding of the compound to at least one of the T2R taste receptors.

36. The method of claim 35, wherein the collection of different T2R taste receptor isoforms are in the form of an array.

37. A specific binding agent capable of discriminating between or among two or more polypeptides of claim 19.

38. The specific binding agent of claim 37, which is an antibody.

39. A method of determining a T2R genotype of a subject, comprising:

obtaining a test sample of DNA containing a T2R sequence of the subject; and

determining whether the subject has a polymorphism in the T2R sequence, wherein the polymorphism is selected from the SNPs referred to as new in Figure 1.

40. A method of identifying a plurality of individuals who are genetically heterogeneous in at least one T2R gene, comprising:

determining a T2R genotype for a plurality of subjects using the method of claim 39; and

selecting group of the subjects who are genetically heterogeneous in at least one T2R gene.

41. The method of claim 40, wherein the plurality of individuals are selected to represent the genetic profile of a geographically defined population.

42. The method of claim 40, wherein the plurality of individuals are selected to represent the genetic profile of Europeans, East Asians, or Africans.

43. A kit for determining whether or not a subject has a selected T2R genotype or haplotype, comprising:

a container comprising at least one oligonucleotide specific for a T2R sequence comprising at least one SNP referred to as new in Figure 1; and

instructions for using the kit, the instructions indicating steps for:

performing a method to detect the presence of variant T2R nucleic acid in the sample; and

analyzing data generated by the method,

wherein the instructions indicate that presence of the variant nucleic acid in the sample indicates that the individual has the selected T2R genotype or haplotype.

44. The kit of claim 43, further comprising a container that comprises a detectable oligonucleotide.

45. A kit for determining whether or not a subject has a selected T2R genotype or haplotype, the kit comprising:

a container comprising a T2R isoform-specific antibody;

a container comprising a negative control sample; and

instructions for using the kit, the instructions indicating steps for:

performing a test assay to detect a quantity of T2R isoform protein in a test sample of tissue and/or bodily fluid from the subject,

performing a negative control assay to detect a quantity of T2R isoform protein in the negative control sample; and

comparing data generated by the test assay and negative control assay,

wherein the instructions indicate that a quantity of T2R isoform protein in the test sample more than the quantity of T2R isoform protein in the negative control sample indicates that the subject has the selected T2R genotype of haplotype, and wherein the T2R isoform-specific antibody is specific for a T2R isoform having a sequence selected from SEQ ID NOs: 50, 56, 58, 60, 64, 66, 68, 70, 72, 76, 78,

80, 82, 84, 86, 90, 92, 94, 96, 100, 102, 104, 106, 108, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 136, 140, 142, 148, 150, 152, 156, 158, 162, 164, 170, 174, 176, 178, 180, 182, 184, 188, 190, 192, 198, 200, 202, 204, 206, 210, 212, 214, 218, 220, 226, 228, 230, 232, 234, 236, 238, 242, 244, 246, 248, 250, 252, 254, 258, 260, and 264.

46. The kit of claim 45 further comprising a container that comprises a detectable antibody that binds to the antibody specific for the T2R isoform protein.

47. A method of screening for a compound useful in influencing T2R taste perception in a mammal, comprising determining if a test compound binds to or interacts with the polypeptide of claim 19 or isolated T2R polypeptide isoform fragment of claim 17, and selecting a compound that so binds.

48 The method of claim 47, wherein binding of the compound inhibits a T2R protein biological activity.

49 The method of claim 47, wherein binding of the compound stimulates a T2R protein biological activity.